PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7 : A61N 1/37, 1/39 — A1

(11) International Publication Number: **WO 00/51680**

(43) International Publication Date: 8 September 2000 (08.09.00)

(21) International Application Number: PCT/US00/05185

(22) International Filing Date: 1 March 2000 (01.03.00)

(30) Priority Data:

60/123,145	5 March 1999 (05.03.99)	US
09/452,533	1 December 1999 (01.12.99)	US

(81) Designated States: CA, JP, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published

With international search report.

Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(71) Applicant: MEDTRONIC, INC. [US/US]; 7000 Central Avenue NE, Minneapolis, MN 55434 (US).

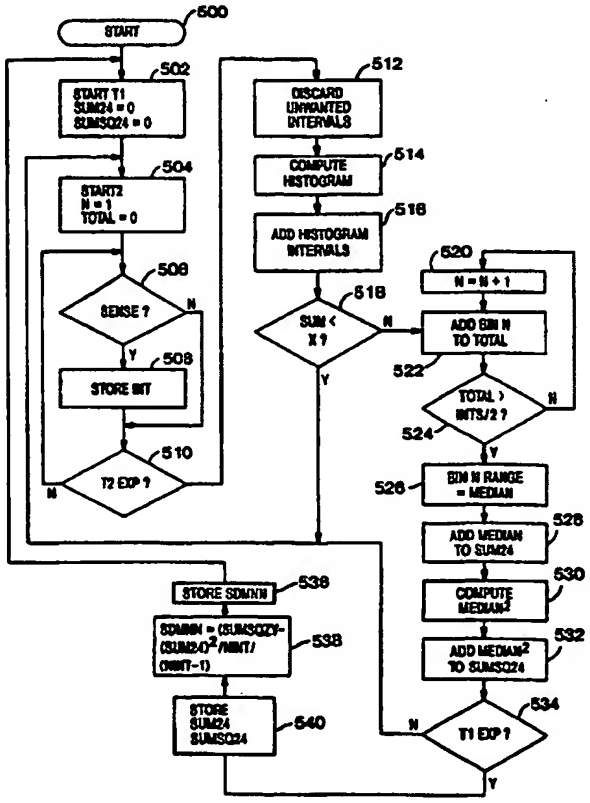
(72) Inventors: PADMANABHAN, Vasant; 8165 Peony Lane North, Maple Grove, MN 55331 (US). OLSON, Walter, H.; 16 Hay Camp Road, North Oaks, MN 55127 (US).

(74) Agents: DUTHLER, Reed, A. et al.; Medtronic, Inc., 7000 Central Avenue NE, Minneapolis, MN 55432 (US).

(54) Title: METHOD AND APPARATUS FOR MONITORING HEART RATE 39

(57) Abstract

An implantable monitoring device for monitoring a patient's heart rate variability over time. The device includes a cardiac electrogram amplifier, a sensing electrode coupled to an input of the amplifier, timing circuitry, processing circuitry and a memory. The timing circuitry defines successive monitoring periods each extending over a period of hours, the monitoring periods together extending at least over a period of weeks and also defines successive shorter time periods during each monitoring period. The memory stores heart intervals between depolarizations of the patient's heart sensed by the amplifier during the shorter time periods. The processing circuitry calculates median intervals between depolarizations of the patient's heart sensed by the amplifier during the shorter time periods and calculates standard deviations of the median intervals calculated during each monitoring period. The processing circuitry may also reject heart intervals occurring during tachyarrhythmias and calculate median intervals based only on heart intervals not rejected.



FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece	ML	Mali	TR	Turkey
BG	Bulgaria	HU	Hungary	MN	Mongolia	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MR	Mauritania	UA	Ukraine
BR	Brazil	IL	Israel	MW	Malawi	UG	Uganda
BY	Belarus	IS	Iceland	MX	Mexico	US	United States of America
CA	Canada	IT	Italy	NE	Niger	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NL	Netherlands	VN	Viet Nam
CG	Congo	KE	Kenya	NO	Norway	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NZ	New Zealand	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	PL	Poland		
CM	Cameroon	KR	Republic of Korea	PT	Portugal		
CN	China	KZ	Kazakstan	RO	Romania		
CU	Cuba	LC	Saint Lucia	RU	Russian Federation		
CZ	Czech Republic	LI	Liechtenstein	SD	Sudan		
DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

BNSDOCID: <WO___0051680A1_I_>

METHOD AND APPARATUS FOR MONITORING HEART RATE

BACKGROUND OF THE INVENTION

The present invention relates generally to implantable medical devices and more particularly to implantable medical devices intended for use in monitoring a patient's heart rhythm.

Implantable pacemakers and cardioverters monitor the heart's rhythm in order to detect arrhythmias and deliver appropriate therapies to terminate detected arrhythmias. In conjunction with this function, the ability of the device is to store information with regard to monitored heart rhythms has dramatically increased over the past two years. Examples of implantable pacemakers and defibrillators which have the capability of storing information related to monitor heart rhythms include U.S. Patent No. 4,223,678 issued to Langer et al., U.S. Patent No. 5,722,999 issued to Snell, U.S. Patent No. 5,513,645 issued to Jacobsen et al. and U.S. Patent No. 5,312,446 issued to Holschbach et al. In addition, there have recently been developed subcutaneously implantable monitoring devices which do not deliver any anti-arrhythmia therapies to the heart but simply store information regarding a patient's heart rhythms for later uplink to an external device. Such devices are disclosed in U.S. Patent No. 5,331,966 issued to Bennett et al., U.S. Patent No. 5,135,004 issued to Adams and U.S. Patent No. 5,497,780 issued to Zehender.

In conjunction with implantable devices as described above, information stored relating to a patient's heart rhythm may include information relating to heart rate trends over time, as disclosed as disclosed in U.S. Patent No. 5,088,488 issued to Markowitz et al., U.S. Patent No. 5,330,513 issued to Nichols et al. and U.S. Patent No. 5,603,331 issued to Heemels et al., as well as information relating to heart rate variability over time, as disclosed in U.S. Patent No.5,749,900 issued to Schroeppel et al., U.S. Patent No.5,466,245 issued to Spinelli et al., U.S. Patent No. 5,411,031 issued to Yomtov et al. and U.S. Patent No. 5,437,285 issued to Verrier et al.

Typically, measurements of heart rate variability in such devices is accomplished employing one of the standard measurements of heart rate variability

such as the SDNN or SDANN indices, described in U.S. Patent No. 5,749,900 issued to Schroeppel et al. and U.S. Patent No. issued to Yomtov, cited above. Unfortunately, obtaining clinically useful information employing the SDNN and SDANN indices traditionally requires the ability to correctly distinguish between normally conducted and ectopic beats, which may be difficult in some circumstances in the context of an implanted device.

SUMMARY OF THE INVENTION

The present invention is directed toward an implanted device having enhanced capabilities for monitoring a patient's heart rate and heart rate variability trends over extended periods of time. The information collected by the implantable device is stored and telemetered to an associated external device such as a device programmer for display and analysis. The collected information and calculated heart rate variability may also be employed to trigger an alarm or alert to the patient, in response to a measured calculation of heart rate variabilty or change in heart rate variability. Heart rates are measured by measuring the time intervals between sensed depolarizations of a chamber of the patient's heart and preceding sensed depolarizations or delivered pacing pulses. Intervals may be measured in the ventricle and/or atrium of the patient's heart. The measured intervals are referred to hereafter as "heart intervals".

In a preferred embodiment of the invention, the device is configured to allow for measurements of heart rate variability trends over extended time periods, employing a measurement of rate variability which does not require the device to accurately distinguish between normally conducted and ectopic beats. In this aspect of the invention, rather than calculating the mean values only of heart intervals beginning and ending in normally conducted beats, the device instead calculates the medians of the stored intervals over short periods of time, including heart intervals beginning or ending in ectopic beats, and calculates the standard deviation of the median values. This difference in calculation methodology produces a measurement of heart rate variability (SDMNN) similar in accuracy to the SDANN index, but

without the requirement of unambiguously identifying ectopic beats and eliminating the heart intervals associated therewith.

In addition, particularly valuable in the context of an implanted device, the process for calculation of a median interval is substantially simplified as opposed to the process for calculating the mean values of the measured intervals with ectopic beats and associated measured intervals excluded. In a preferred embodiment of the invention, the process of calculation of the median is further simplified by first producing a histogram of the stored heart interval values, sorting the intervals into bins each associated with an interval range. The numbers of intervals in each bin are then successively added to one another until the total exceeds half of the total number of intervals binned and the rate range associated with the last bin added is employed to define the median interval value.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 illustrates an implantable pacemaker/cardioverter/ defibrillator of a type useful in practicing the present invention, in conjunction with a human heart.

Figure 2 illustrates an implantable pacemaker of a type useful in practicing the present invention, in conjunction with a human heart.

Figure 3 illustrates an implantable monitor of a type useful in practicing the present invention.

Figure 4 is a perspective view of a programmer of a type useful in practicing the present invention.

Figure 5 is a functional schematic diagram of an implantable pacemaker/cardioverter/defibrillator of a type useful in practicing the present invention.

Figure 6 is a functional schematic diagram of an implantable pacemaker of a type useful in practicing the present invention.

Figure 7 is a functional schematic diagram of an implantable monitor of a type useful in practicing the present invention.

Figure 8 is a functional schematic diagram of a programmer of a type useful in practicing the present invention.

Figure 9 is a functional flow chart illustrating a method of monitoring heart rate variability which may be employed in conjunction with the present invention.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

Figure 1 illustrates a defibrillator and lead set of a type in which the present invention may usefully be practiced. The ventricular lead includes an elongated insulative lead body 16, carrying three mutually insulated conductors. Located adjacent the distal end of the lead are a ring electrode 24, an extendable helix electrode 26, mounted retractably within an insulative electrode head 28, and an elongated coil electrode 20. Each of the electrodes is coupled to one of the conductors within the lead body 16. Electrodes 24 and 26 are employed for cardiac pacing and for sensing ventricular depolarizations. At the proximal end of the lead is a bifurcated connector 14 which carries three electrical connectors, each coupled to one of the coiled conductors.

The atrial/SVC lead includes an elongated insulative lead body 15, also carrying three mutually insulated conductors. Located adjacent the J-shaped distal end of the lead are a ring electrode 21 and an extendible helix electrode 17, mounted retractably within an insulative electrode head 19. Each of the electrodes is coupled to one of the conductors within the lead body 15. Electrodes 17 and 21 are employed for atrial pacing and for sensing atrial depolarizations. An elongated coil electrode 23 is provided, proximal to electrode 21 and coupled to the third conductor within the lead body 15. At the proximal end of the lead is a bifurcated connector 13 which carries three electrical connectors, each coupled to one of the coiled conductors.

The coronary sinus lead includes an elongated insulative lead body 6, carrying one conductor, coupled to an elongated coiled defibrillation electrode 8. Electrode 8, illustrated in broken outline, is located within the coronary sinus and great vein of the heart. At the proximal end of the lead is a connector plug 4 which carries an electrical connector, coupled to the coiled conductor.

The pacemaker/cardioverter/defibrillator 10 includes a hermetic enclosure 11 containing the electronic circuitry used for generating cardiac pacing pulses for delivering cardioversion and defibrillation shocks and for monitoring the patient's heart rhythm. Pacemaker/cardioverter/defibrillator 10 is shown with the lead connector assemblies 4, 13 and 14 inserted into the connector block 12 which serves as a receptacle and electrical connector for receiving the connectors 4, 13 and 14 and interconnecting the leads to the circuitry within enclosure 11. An activity sensor 30 is illustrated schematically by broken outline, and may be an accelerometer or a piezoelectric transducer. Sensor 30 may be used for regulation of pacing rate based upon demand for cardiac output.

Optionally, insulation of the outward facing portion of the housing 11 of the pacemaker/cardioverter/defibrillator 10 may be provided or the outward facing portion may instead be left uninsulated, or some other division between insulated and uninsulated portions may be employed. The uninsulated portion of the housing 11 optionally serves as a subcutaneous defibrillation electrode, used to defibrillate either the atria or ventricles. Other lead configurations and electrode locations may of course be substituted for the lead set illustrated. For example, atrial defibrillation and sensing electrodes might be added to either the coronary sinus lead or the right ventricular lead instead of being located on a separate atrial lead, allowing for a two-lead system.

Figure 2 illustrates a cardiac pacemaker of a type appropriate for use in practicing the present invention in conjunction with its associated lead system, illustrated in relation to a patient's heart. The pacemaker 120 includes a hermetic enclosure 124 containing the electronic circuitry used for generating cardiac pacing pulses and for monitoring the patient's heart rhythm. An activity sensor 126 is illustrated schematically by broken outline, and may be an accelerometer or a piezoelectric transducer as discussed above in conjunction with Figure 1. Mounted to the enclosure 124 is a header 122 which serves as a receptacle and electrical connector for receiving the connectors 132 and 134 of pacing leads 128 and 130 and interconnecting the leads to the circuitry within enclosure 124. Lead 128 is a

ventricular lead provided with electrodes 140 and 142 for monitoring right ventricular heart signals. Also illustrated on lead 128 is a physiologic sensor 144 which may optionally be included in addition to or as an alternative to the activity sensor 126, and which may take the form of an oxygen sensor, pressure sensor, temperature sensor, other sensor of any of the various types employed for monitoring demand for cardiac output or for measuring heart hemodynamics. Sensor 124 may be used in conjunction with or as an alternative to the activity sensor 126 for rate responsive pacing. Atrial lead 130 carries electrodes 136 and 138 and is employed for sensing and pacing the patient's atrium.

Figure 3 illustrates a subcutaneously implantable monitor of a type appropriate for use in practicing the present invention. The monitor shares the external configuration of the Medtronic Reveal® implantable monitor, and is provided with a hermetically sealed enclosure 104 containing the electronic circuitry used for generating cardiac pacing pulses and for monitoring the patient's heart rhythm and which carries a molded plastic header 108. The enclosure 104 and the header 108 each carry an electrode 102 and 106, respectively for monitoring heart rhythm. Also mounted in the header 108 is an antenna 110 for use in communicating between the device and an external programmer. Illustrated in broken outline at 112 is an internal activity sensor, of the type typically employed in the context of rate responsive cardiac pacemakers, taking the form either of an accelerometer or a piezo-electric transducer. Heart signals are detected between the electrodes 102 and 106 and measurements of physical activity are detected by sensor 112 for storage and analysis.

Figure 4 is a plan view of an external programmer of a sort appropriate for use in conjunction with the practice of the present invention in conjunction with any of the devices of Figures 1 - 3. The programmer 420 is a microprocessor controlled device which is provided with a programming head 422 for communicating with an implanted device, a set of surface electrogram electrodes 459 for monitoring a patient's electrogram, a display 455 which is preferably a touch sensitive display, control buttons or keys 465, and a stylist 456 for use in conjunction with the touch sensitive screen 455. By means of the control keys 465 and the touch sensitive screen

455 and stylus 456, the physician may format commands for transmission to the implantable device. By means of the screen 455, the physician may observe information telemetered from the implantable device. The programmer is further provided with a printer 463 which allows for hard copy records of displays of signals received from the implanted device such as electrograms, stored parameters, programmed parameters and information as to heart rate variability trends according to the present invention. While not visible in this view, the device may also be provided with a floppy disk or CD ROM drive and/or a port for insertion of expansion cards such as P-ROM cartridges, to allow for software upgrades and modifications to the programmer 420.

In the context of the present invention, programmer 420 may serve simply as a display device, displaying information with regard to heart rate variability as calculated by the implanted device or instead may receive uplinked raw data related to heart intervals and may calculate the heart rate trends and heart rate variability values according to the present invention. It is believed that it is preferable for the implanted device to perform the bulk of the computations necessary to practice the invention, and in particular that it is preferable for the implanted device to at least calculate median rate values, to reduce the storage requirements within the implanted device. However, allocation of functions between the implanted device and the programmer may differ from the preferred embodiments and still result in a workable system.

Figure 5 is a functional schematic diagram of an implantable pacemaker/cardioverter/defibrillator of the type illustrated in Figure 3, in which the present invention may usefully be practiced. This diagram should be taken as exemplary of one type of anti-tachyarrhythmia device in which the invention may be embodied, and not as limiting, as it is believed that the invention may usefully be practiced in a wide variety of device implementations, including devices providing therapies for treating atrial arrhythmias instead of or in addition to ventricular arrhythmias, cardioverters and defibrillators which do not provide anti-tachycardia pacing therapies, anti-tachycardia pacers which do not provide cardioversion or

defibrillation, and devices which deliver different forms of anti-arrhythmia therapies such nerve stimulation or drug administration.

The device is provided with a lead system including electrodes, which may be as illustrated in Figure 1. Alternate lead systems may of course be substituted. If the electrode configuration of Figure 1 is employed, the correspondence to the illustrated electrodes is as follows. Electrode 311 corresponds to electrode 11, and is the uninsulated portion of the housing of the implantable pacemaker/cardioverter /defibrillator. Electrode 320 corresponds to electrode 20 and is a defibrillation electrode located in the right ventricle. Electrode 310 corresponds to electrode 8 and is a defibrillation electrode located in the coronary sinus. Electrode 318 corresponds to electrode 28 and is a defibrillation electrode located in the superior vena cava. Electrodes 324 and 326 correspond to electrodes 24 and 26, and are used for sensing and pacing in the ventricle. Electrodes 317 and 321 correspond to electrodes 19 and 21 and are used for pacing and sensing in the atrium.

Electrodes 310 , 311, 318 and 320 are coupled to high voltage output circuit 234. Electrodes 324 and 326 are coupled to the R-wave amplifier 200, which preferably takes the form of an automatic gain controlled amplifier providing an adjustable sensing threshold as a function of the measured R-wave amplitude. A signal is generated on R-out line 202 whenever the signal sensed between electrodes 324 and 326 exceeds the present sensing threshold.

Electrodes 317 and 321 are coupled to the P-wave amplifier 204. which preferably also takes the form of an automatic gain controlled amplifier providing an adjustable sensing threshold as a function of the measured R-wave amplitude. A signal is generated on P-out line 206 whenever the signal sensed between electrodes 317 and 321 exceeds the present sensing threshold. The general operation of the R-wave and P-wave amplifiers 200 and 204 may correspond to that disclosed in U.S. Patent No. 5,117,824, by Keimel, et al., issued June 2, 1992, for an Apparatus for Monitoring Electrical Physiologic Signals, incorporated herein by reference in its entirety. However, any of the numerous prior art sense amplifiers employed in

implantable cardiac pacemakers, defibrillators and monitors may also usefully be employed in conjunction with the present invention.

Switch matrix 208 is used to select which of the available electrodes are coupled to wide band amplifier 210 for use in digital signal analysis. Selection of electrodes is controlled by the microprocessor 224 via data/address bus 218, which selections may be varied as desired. Signals from the electrodes selected for coupling to bandpass amplifier 210 are provided to multiplexer 220, and thereafter converted to multi-bit digital signals by A/D converter 222, for storage in random access memory 226 under control of direct memory access circuit 228. Microprocessor 224 may employ digital signal analysis techniques to characterize the digitized signals stored in random access memory 226 to recognize and classify the patient's heart rhythm employing any of the numerous signal processing methodologies known to the art.

Telemetry circuit 330 receives downlink telemetry from and sends uplink telemetry to the patient activator by means of antenna 332. Data to be uplinked to the activator and control signals for the telemetry circuit are provided by microprocessor 224 via address/data bus 218. Received telemetry is provided to microprocessor 224 via multiplexer 220. The atrial and ventricular sense amp circuits 200, 204 produce atrial and ventricular EGM signals which also may be digitized and uplink telemetered to an associated programmer on receipt of a suitable interrogation command. The device may also be capable of generating so-called marker codes indicative of different cardiac events that it detects. A pacemaker with marker-channel capability is described, for example, in U.S. Patent No. 4,374,382 to Markowitz, which patent is hereby incorporated by reference herein in its entirety. The particular telemetry system employed is not critical to practicing the invention, and any of the numerous types of telemetry systems known for use in implantable devices may be used. In particular, the telemetry systems as disclosed in U.S. Patent No. 5,292,343 issued to Blanchette et al., U.S. Patent No. 5,314,450, issued to Thompson, U.S. Patent No. 5,354,319, issued to Wyborny et al. U.S. Patent No. 5,383,909, issued to Keimel, U.S. Patent No. 5,168,871, issued to Grevious, U.S. Patent No. 5,107,833 issued to Barsness or U.S. Patent No. 5,324,315, issued to

Grevious, all incorporated herein by reference in their entireties, are suitable for use in conjunction with the present invention. However, the telemetry systems disclosed in the various other patents cited herein which are directed to programmable implanted devices, or similar systems may also be substituted. The telemetry circuit 330 is of course also employed for communication to and from an external programmer, as is conventional in implantable anti-arrhythmia devices.

The device of Figure 5 may additionally is provided with an activity sensor 344, mounted to the interior surface of the device housing or to the hybrid circuit within the device housing. The sensor 344 and sensor present in circuitry 342 may be employed in the conventional fashion described in U.S. Patent 4,428,378 issued to Anderson et al, incorporated herein by reference in its entirety, to regulate the underlying pacing rate of the device in rate responsive pacing modes.

The remainder of the circuitry is dedicated to the provision of cardiac pacing, cardioversion and defibrillation therapies, and, for purposes of the present invention may correspond to circuitry known in the prior art. An exemplary apparatus is disclosed for accomplishing pacing, cardioversion and defibrillation functions as follows. The pacer timing/control circuitry 212 includes programmable digital counters which control the basic time intervals associated with DDD, VVI, DVI, VDD, AAI, DDI, DDDR, VVIR, DVIR, VDDR, AAIR, DDIR and other modes of single and dual chamber pacing well known to the art. Circuitry 212 also controls escape intervals associated with anti-tachyarrhythmia pacing in both the atrium and the ventricle, employing, any anti-tachyarrhythmia pacing therapies known to the art.

Intervals defined by pacing circuitry 212 include atrial and ventricular pacing escape intervals, the refractory periods during which sensed P-waves and R-waves are ineffective to restart timing of the escape intervals and the pulse widths of the pacing pulses. The durations of these intervals are determined by microprocessor 224, in response to stored data in memory 226 and are communicated to the pacing circuitry 212 via address/data bus 218. Pacer circuitry 212 also determines the amplitude of the cardiac pacing pulses under control of microprocessor 224.

During pacing, the escape interval counters within pacer timing/control circuitry 212 are reset upon sensing of R-waves and P-waves as indicated by signals on lines 202 and 206, and in accordance with the selected mode of pacing on time-out trigger generation of pacing pulses by pacer output circuits 214 and 216, which are coupled to electrodes 317, 321, 324 and 326. The escape interval counters are also reset on generation of pacing pulses, and thereby control the basic timing of cardiac pacing functions, including anti-tachyarrhythmia pacing.

The durations of the intervals defined by the escape interval timers are determined by microprocessor 224, via data/address bus 218. The value of the count present in the escape interval counters when reset by sensed R-waves and P-waves may be used to measure the durations of R-R intervals, P-P intervals, PR intervals and R-P intervals, which measurements are stored in memory 226 and are used in conjunction with the present invention to measure heart rate variability and in conjunction with tachyarrhythmia detection functions.

Microprocessor 224 operates as an interrupt driven device, and is responsive to interrupts from pacer timing/control circuitry 212 corresponding to the occurrences of sensed P-waves and R-waves and corresponding to the generation of cardiac pacing pulses. These interrupts are provided via data/address bus 218. Any necessary mathematical calculations to be performed by microprocessor 224 and any updating of the values or intervals controlled by pacer timing/control circuitry 212 take place following such interrupts. Microprocessor 224 includes associated ROM in which the stored program controlling its operation as described below resides. A portion of the memory 226 (Figure 2) may be configured as a plurality of recirculating buffers, capable of holding series of measured intervals, which may be analyzed in response to the occurrence of a pace or sense interrupt to determine whether the patient's heart is presently exhibiting atrial or ventricular tachyarrhythmia.

The arrhythmia detection method of the present invention may include any of the numerous available prior art tachyarrhythmia detection algorithms. One preferred embodiment may employ all or a suset of the rule-based detection methods described in U.S. Patent No. 5,545,186 issued to Olson et al. or in U.S. Patent No. 5,755,736

issued to Gillberg et al., both incorporated herein by reference in their entireties. However, any of the various arrhythmia detection methodologies known to the art might also usefully be employed in alternative embodiments of the invention.

In the event that an atrial or ventricular tachyarrhythmia is detected, and an anti-tachyarrhythmia pacing regimen is desired, timing intervals for controlling generation of anti-tachyarrhythmia pacing therapies are loaded from microprocessor 224 into the pacer timing and control circuitry 212, to control the operation of the escape interval counters therein and to define refractory periods during which detection of R-waves and P-waves is ineffective to restart the escape interval counters.

In the event that generation of a cardioversion or defibrillation pulse is required, microprocessor 224 employs the escape interval counter to control timing of such cardioversion and defibrillation pulses, as well as associated refractory periods. In response to the detection of atrial or ventricular fibrillation or tachyarrhythmia requiring a cardioversion pulse, microprocessor 224 activates cardioversion/defibrillation control circuitry 230, which initiates charging of the high voltage capacitors 246, 248 via charging circuit 236, under control of high voltage charging control line 240. The voltage on the high voltage capacitors is monitored via VCAP line 244, which is passed through multiplexer 220 and in response to reaching a predetermined value set by microprocessor 224, results in generation of a logic signal on Cap Full (CF) line 254, terminating charging. Thereafter, timing of the delivery of the defibrillation or cardioversion pulse is controlled by pacer timing/control circuitry 212. Following delivery of the fibrillation or tachycardia therapy the microprocessor then returns the device to cardiac pacing and awaits the next successive interrupt due to pacing or the occurrence of a sensed atrial or ventricular depolarization. In the illustrated device, delivery of the cardioversion or defibrillation pulses is accomplished by output circuit 234, under control of control circuitry 230 via control bus 238. Output circuit 234 determines whether a monophasic or biphasic pulse is delivered, whether the housing 311 serves as cathode or anode and which electrodes are involved in delivery of the pulse.

Figure 6 is a functional schematic diagram of the pacemaker 120 illustrated in Figure 2. The pacemaker of Figures 2 and 6 is essentially a set of subcomponents of the implantable pacemaker/cardioverter/defibrillator illustrated in Figures 1 and 5. Like the device of Figure 5, the pacemaker is a microprocessor controlled device with microprocessor 189 operating under control of programming stored in Read Only Memory (ROM) 191. In the device as illustrated, electrodes 136 and 138, intended for location in the atrium of the patient's heart are coupled to an atrial amplifier 181 which may correspond to atrial amplifier 204 in Figure 5. Similarly, ventricular electrodes 140 and 142 are coupled to ventricular amplifier 182, which may correspond to ventricular amplifier 200 in Figure 5. The outputs of atrial and ventricular amplifiers 181 and 182 are input into timing and control circuitry 183 which conforms generally to the pacer timing and control circuitry 212 of Figure 5, and which measures intervals between detected depolarizations and controls intervals between delivered pacing pulses as well as generating interrupts via data/address 192 to awake microprocessor 189 in response to delivery of a pacing pulse or sensing of a cardiac depolarization. Intervals between depolarizations measured by timing/control circuitry 183 are stored in Random Access Memory (RAM) 190 until processed by microprocessor 189 to derive average heart rate values. Atrial and ventricular pacing pulses delivered according to one or more of the standard pacing modes described in conjunction with Figure 5 are produced by atrial and ventricular pulse generator circuits 184 and 185 which may correspond to pulse generator circuits 215 ad 216 in Figure 5.

The sensor illustrated in Figure 6 may correspond to either an activity sensor 126 as described in conjunction with Figure 2 above or to a hemodynamic sensor 140, as described in conjunction with Figure 2. If the sensor is an activity sensor, then sensor processing circuitry 186 may correspond to sensor processing circuitry 342 discussed in conjunction with Figure 5. However, if the sensor is a hemodynamic sensor, the sensor processing circuitry would correspond to the sort of processing circuitry typically associated with hemodynamic sensors. Telemetry circuitry 187 in conjunction with antenna 188 serves to transmit information to and receive

information from an external programmer precisely as described above in conjunction with the device of Figure 5, including information related to stored median interval values and heart rate variability measurements in RAM 190, as calculated by microprocessor 189.

Figure 7 illustrates the functional organization of the subcutaneously implantable heart monitor 100 illustrated in Figure 3. This device consists essentially of a set of subcomponents of the more complex embodiment of the invention disclosed in Figure 5, and includes a sense amplifier 152 coupled to electrodes 102 and 106, illustrated in Figure 1. Sense amplifier 152 may correspond to sense amplifier 204 or 200 in Figure 5. Like the device of Figure 5, the implantable monitor may be a microprocessor control device operating under control microprocessor 156 with its functionality controlled primarily by software stored in the read only memory associated therein. In this context, amplifier 152 detects the occurrence of heart depolarizations, with timing/control circuitry 154 serving to measure the durations between the detected heart depolarizations and to generate interrupts awakening microprocessor 156 so that it may store, analyze and process the detected intervals. Random Access Memory (RAM) 158 serves to store measured and calculated parameters including the calculated median heart rate and/or heart rate variability values for later telemetry to an external device. Like the device in Figure 5, timing and control circuitry communicates with the microprocessor and the remaining circuitry by means of the address/data bus 168. Telemetry system 162 may correspond to telemetry system 330 in Figure 5 and, via antenna 110 transmits and receives information from the external programmer, including transmitting information with regard to the calculated median rate values and heart variability values stored in RAM 158. Sensor 112 may correspond to sensor 344 in Figure 5 and it may be a physical activity sensor as discussed above. The output of sensor 112 is passed through sensor processing circuitry 166 which may correspond to sensor processing circuitry 342 in Figure 5.

Figure 8 is a functional schematic of a programmer as illustrated in Figure 4 appropriate for use in conjunction with the invention. Programmer 420 is a personal

computer type, microprocessor-based device incorporating a central processing unit 450, which may be, for example, an Intel 80386 or 80486 or Pentium microprocessor or the like. A system bus 451 interconnects CPU 450 with a hard disk drive 452 storing operational programs and data and with a graphics circuit 453 and an interface controller module 454. A floppy disk drive 466 or a CD ROM drive is also coupled to bus 451 and is accessible via a disk insertion slot within the housing of the programmer 420. Programmer 420 further comprises an interface module 457 which includes digital circuit 458, non-isolated analog circuit 459, and isolated analog circuit 460. Digital circuit 448 enables interface module 457 to communicate with interface controller module 454.

In order for the physician or other care giver or user to communicate with the programmer 420, control buttons 465 or optionally a keyboard coupled to CPU 50 are provided. However the primary communication mode is through graphics display screen 455 of the well-known "touch sensitive" type controlled by graphics circuit 453. A user of programmer 420 may interact therewith through the use of a stylus 456, also coupled to graphics circuit 453, which is used to point to various locations on screen 455 which display menu choices for selection by the user or an alphanumeric keyboard for entering text or numbers and other symbols.

Graphics display 455 also displays a variety of screens of telemetered out data or real time data including measurements of heart rate variability and heart rate trends according to the present invention. Programmer 420 is also provided with a strip chart printer 463 or the like coupled to interface controller module 454 so that a hard copy of a patient's ECG, EGM, marker channel or of graphics displayed on the display 455 can be generated.

As will be appreciated by those of ordinary skill in the art, it is often desirable to provide a means for programmer 20 to adapt its mode of operation depending upon the type or generation of implanted medical device to be programmed. Accordingly, it may be desirable to have an expansion cartridge containing EPROMs or the like for storing software programs to control programmer 420 to operate in a particular manner corresponding to a given type or generation of implantable medical device. In

addition, in accordance with the present invention, it is desirable to provide the capability through the expansion cartridge or through the floppy disk drive 66 or CD ROM drive.

The non-isolated analog circuit 459 of interface module 457 is coupled to a programming head 422 which is used to establish the uplink and downlink telemetry links between the pacemaker 410 and programmer 420 as described above. Uplink telemetered EGM signals are received in programming head 422 and provided to non-isolated analog circuit 459. Non-isolated analog circuit 459, in turn, converts the digitized EGM signals to analog EGM signals and presents these signals on output lines A EGM OUT and V EGM OUT. These output lines may then be applied to a strip-chart recorder 463 to provide a hard-copy printout of the A EGM or V EGM for viewing by the physician. Similarly, the markers be received by programming head 422 are presented on the MARKER CHANNEL output line from non-isolated analog circuit 459.

Isolated analog circuit 460 in interface module 547 is provided to receive external ECG and electrophysiologic (EP) stimulation pulse signals. In particular, analog circuit 460 receives ECG signals from patient skin electrodes 459 and processes these signals before providing them to the remainder of the programmer system in a manner well known in the art. Circuit 460 further operates to receive the EP stimulation pulses from an external EP stimulator for the purposes of non-invasive EP studies, as is also known in the art.

In order to ensure proper positioning of programming head 422 over the antenna of the associated implanted device, feedback is provided to the physician that the programming head 422 is in satisfactory communication with and is receiving sufficiently strong RF signals. This feedback may be provided, for example, by means of a head position indicator, e.g. a light-emitting diode (LED) or the like that is lighted to indicate a stable telemetry channel.

Figure 9 is a functional flow chart illustrating the overall method of operation of a device according to the present invention in monitoring heart intervals and in calculating an index of heart rate variability for display on external programmer. In

conjunction with the flow chart of Figure 9, it should be understood that the operations illustrated are all presumed to take place in the implanted device, which is believed to be a preferred embodiment of the invention. In this context, it should also be understood that all calculations and processing of the measured heart intervals is performed by the microprocessor within the implanted device. However, in alternative embodiments, one or more steps of the method for determining an index of heart rate variability may be performed in the external device, based on information telemetered to the external device by the implanted device.

After initialization at 500, at 502 the device starts time period T1 which corresponds to a prolonged time period over which heart rate variability is to be determined, and typically will be a period of hours or days. Most preferably, it is believed that T1 should correspond to a period of a single day for ease in display and understanding of the calculated heart rate variability values. In conjunction with initiation of time period T1, the value of SUM 24 and SUM SQ24 are both reset to 0. SUM 24 is intended to reflect the sum of all calculated median values of heart intervals separating depolarizations of the chamber of the heart, e.g. atrial or ventricular depolarizations, over the 24 hour period. SUM SQ24 reflects a sum of the squares of the median values of the heart intervals taken over the 24 hour period. These values will be incremented with the expiration of each of a number of shorter time periods T2, and will be employed to calculate the observed heart rate variability over time period T1 using the SDMNN heart rate variability index according to the present invention. At 504, the device initiates the first of a sequence of shorter time periods T2 which may be, for example, periods of one to 20 minutes, preferably about 5 minutes. The median of value of the heart intervals between successive depolarizations during these 5 minute periods are employed to calculate the value of SUM24 and SUMSQ24, described above. In addition, at 504 the device resets the value N, corresponding to a bin of a histogram of stored heart intervals, to 1. This value will be incremented and employed in calculating the median interval during each of the shorter time periods T2, as discussed below. The value of TOTAL, also employed in calculating the value of the median interval as discussed below is also

reset to zero at 504. During T2, in response to a sensed depolarization at 506, the device collects the heart interval ending with the sensed depolarization at 508. On expiration of T2 at 510, the device proceeds to determine whether a median value for the collected heart intervals during T2 can be usefully calculated, and if so, proceeds to calculate the median interval value. This is accomplished by first optionally discarding unwanted heart intervals at 510. Whether this step will be necessary or not is a function of the type of device employed to monitor heart rate variability and the status of the patient in whom the device is implanted. For example, in the case of a patient who is subject to atrial or ventricle tachycardia, wherein the device employing the present invention is an implantable pacemaker or pacemaker/cardioverter/defibrillator, it may be desirable to discard all intervals beginning with a paced depolarization. It may also be desirable to discard all heart intervals associated with detection and treatment of tachyarrhythmias. For example all heart intervals which meet tachyarrhythmia detection criteria due to their relatively short duration, all intervals obtained during charging of the output capacitors of such a device prior to delivery of a cardioversion or defibrillation shock and all intervals sensed during delivery of anti-tachyarrhythmia therapies such as anti-tachycardia pacing, cardioversion and defibrillation may be discarded. In addition or as an alternative, in cases in which the invention is embodied in the context of a dual chamber pacemaker capable of switching between various pacing modes in response to detected atrial tachyarrhythmias, it may be desirable to discard heart intervals measured during operation of the mode switch between pacing modes. In contrast, if the patient has a simple VVI type pacemaker, and is not subject to tachyarrhythmias, there may be no need to discard any collected heart intervals except those beginning in paced depolarizations. It should be noted that even if some or all of these heart intervals are to be discarded, selection of intervals to be discarded does not require the ability to distinguish between normally conducted and ectopic beats, but only the ability to either measure the durations between depolarizations and/or the underlying operative states of the device. At 514, the retained heart intervals are arranged into a histogram divided into a desired number of bins based on interval duration. For

example, the histogram may be divided into 130 bins, each ten milliseconds wide, extending from 300 milliseconds through 1600 milliseconds. Intervals less than 300 milliseconds may be binned in the 300-310 millisecond bin, while intervals greater than 1600 milliseconds may be binned in the 1590 -1600 milliseconds bin. In order to minimize data storage required for the histogram, the value of the number of intervals in a bin may optionally be limited to a maximum value, for example, 750.

After the device produces the histogram of intervals and stores it in the random access memory (RAM) of the device, the device at 516 adds the values of all binned intervals within the histogram. At 518, the device checks the value of the sum of the binned intervals against a preset total duration which may be a proportion of the value of the duration of time period T2. For example, the device may require that the total duration of the intervals within the histogram bins is at least 20% of the duration of time period T2. If the total duration binned heart intervals are less than this value, there is no calculation of a median for the preceding time period T2, and the device begins the timing of the next time period T2 at 504. If, however, the cumulative total of the binned intervals is sufficiently great at 518, the device then calculates a median interval value by first adding the number of intervals in bin N (previously initialized to 1) to the value of TOTAL (previously initialized to 0). At 524 the device checks to determine whether TOTAL is more than one half of the total number (NINT) of intervals binned. If not, the value of N is incremented to 520 and the number of intervals in the next bin are added to TOTAL at 522, until TOTAL exceeds half the total number of intervals binned. At this point, at 526, the rate range associated with bin N (the last bin whose intervals were added to the value of TOTAL) serves to define the median heart rate during the preceding time period T2. The lower end of the range of the bin, the upper end of the range of the bin, or more preferably the middle of the range associated with the bin may be employed as the median. At 528 the value of the calculated median is added to SUM 24. At 530 the value of the median is squared, and the square of the median is added to SUMSQ24 at 532.

If the longer time period T1 has not expired at 534, the device returns to restart timing of the next shorter period T2 at 504 and continues to collect heart rate intervals

and calculate interval medians until expiration of the longer time period T1. Following the expiration of the longer time period T1 at 534, the device proceeds to calculate the index of heart rate variability SDMNN according to the present invention by first storing the calculated values of SUM24 and SUMSQ24 at 540. The value of SDMNN is calculated at 538, according to the formula SDMNN = (SUMSQ24 - $(SUM24)^2$/NINT)/(NINT - 1). This value is then stored in the implanted device for later telemetry to an external device.

As noted above, it is believed that in some cases the allocation of functions between the external and internal device employed to practice the invention may be somewhat different. For example, instead of actually calculating the value of SDMNN according to the present invention, the implanted device may simply store the values of SUM24 and SUMSQ24, so that the external device may later perform the calculation of SDMNN according to the present invention. It is also possible that in some embodiments, the device may simply collect the values of undiscarded heart intervals, for later uplinking to external device wherein the calculation of median values and the heart rate variability index SDMNN may thereafter be undertaken. However, this embodiment is believed less desirable in that it requires substantial additional data storage base within the implanted device.

In conjunction with the above disclosure, we claim:

Claims:

1. An implantable monitoring device for monitoring a patient's heart rate variability over time, comprising:

a cardiac electrogram amplifier;

a sensing electrode coupled to an input of the amplifier;

timing means comprising means for defining successive monitoring periods each extending over a period of hours, the monitoring periods together extending at least over a period of weeks and means for defining successive shorter time periods during each monitoring period;

memory means for storing heart intervals between depolarizations of the patient's heart sensed by the amplifier during the shorter time periods;

calculating means comprising means for calculating median intervals between depolarizations of the patient's heart sensed by the amplifier during the shorter time periods and means for calculating standard deviations of the median intervals calculated during each monitoring period.

2. A device according to claim 1, further comprising means for rejecting heart intervals occurring during tachyarrhythmias and wherein the calculating means comprises means for calculating median intervals based only on heart intervals not rejected.

3. A device according to claim 2 wherein the calculating means comprises means for determining total durations of non-rejected heart intervals during the shorter time intervals and means for preventing calculation of a median interval if the total duration of non-rejected heart intervals during a shorter time period is less that a required duration.

4. A device according to claim 1 wherein the calculating means comprises means for binning stored heart intervals into a histogram comprising multiple bins each

associated with a heart interval range, means for successively adding numbers of intervals stored in the bins until a sum is reached which exceeds one half of total intervals in the bins and means responsive to the sum exceeding one half of total intervals in the bins for designating as a median interval an interval associated with the interval range of the bin having the number of intervals stored therein most recently added to the sum.

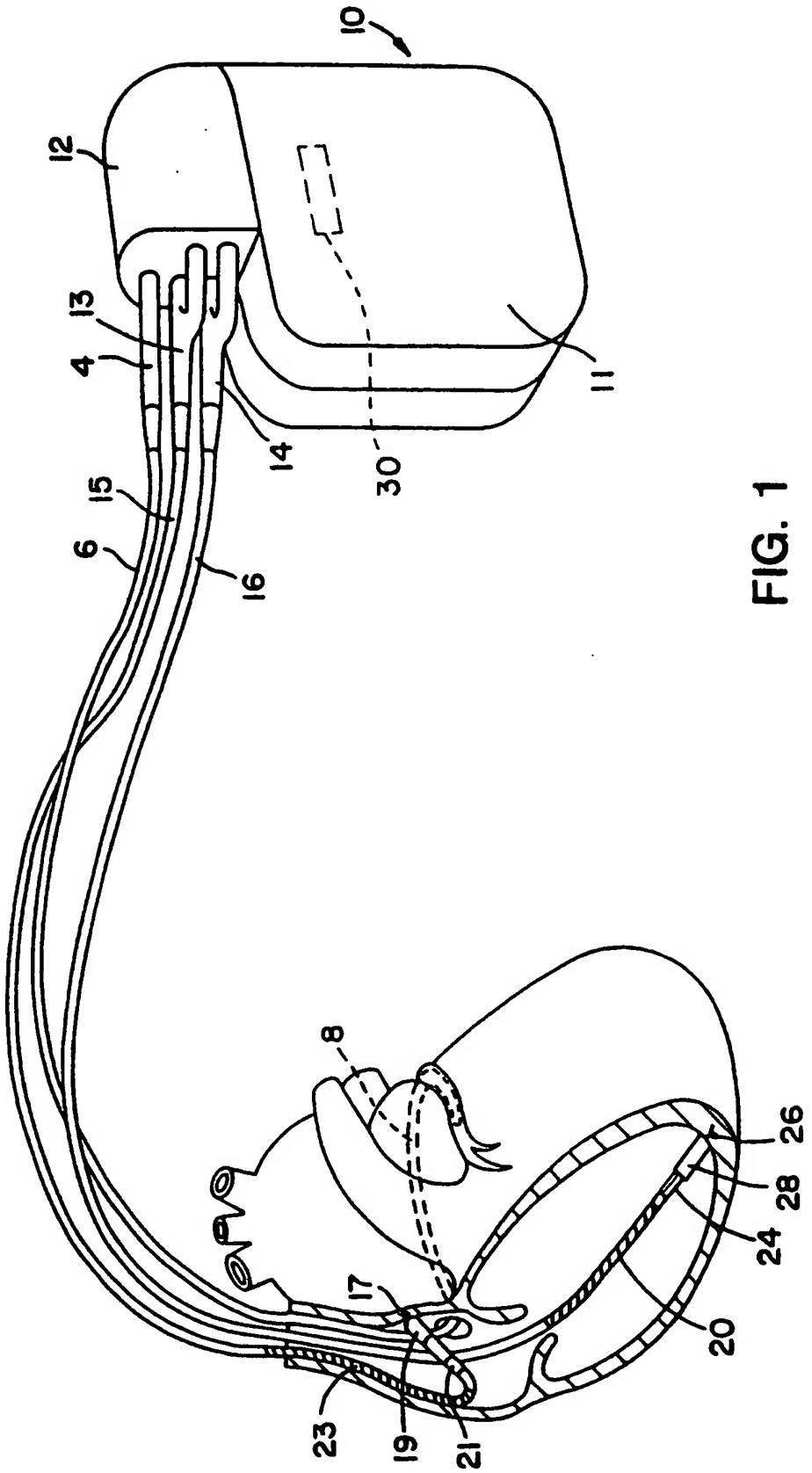


FIG. 1

BNSDOCID: <WO__0051680A1_I_>

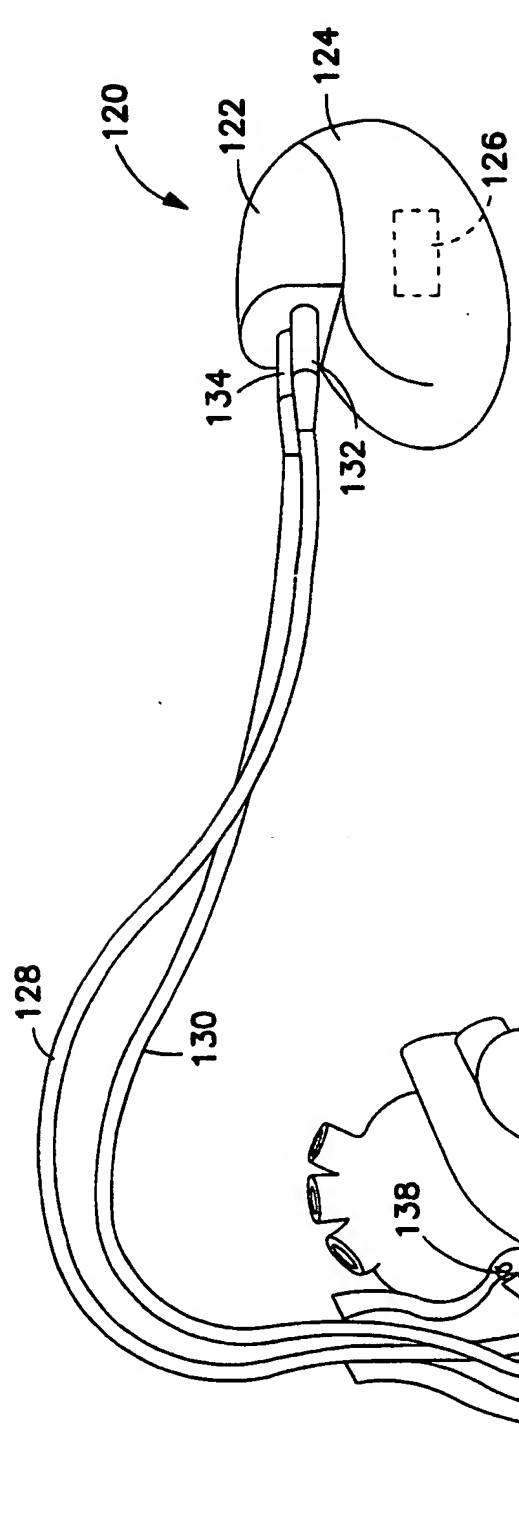


FIG. 2

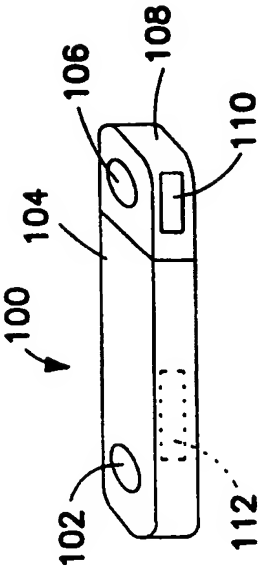


FIG. 3

ENSDOCID: <WO___0051680A1_I_>

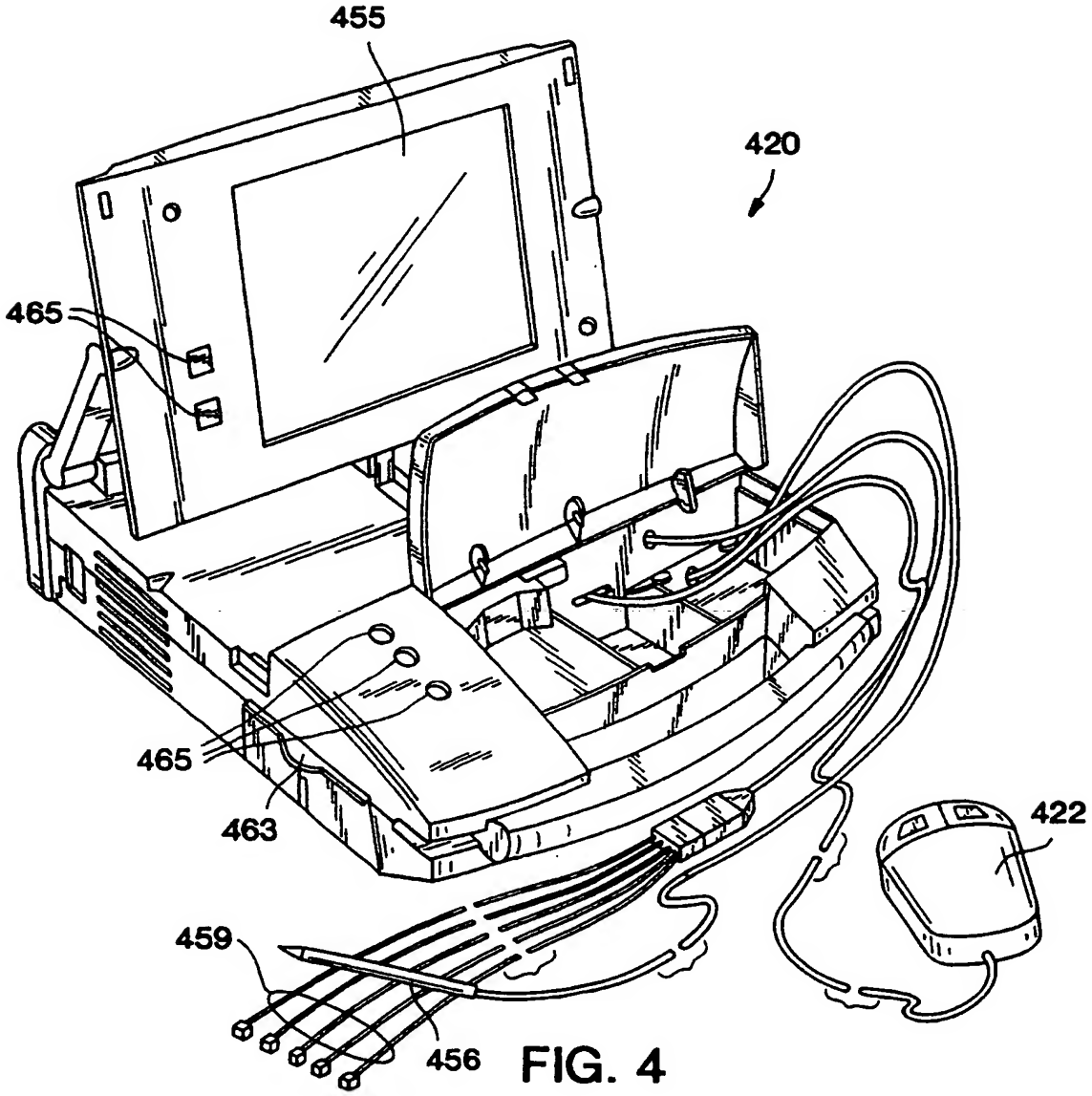


FIG. 4

BNSDOCID: <WO___0051680A1_I_>

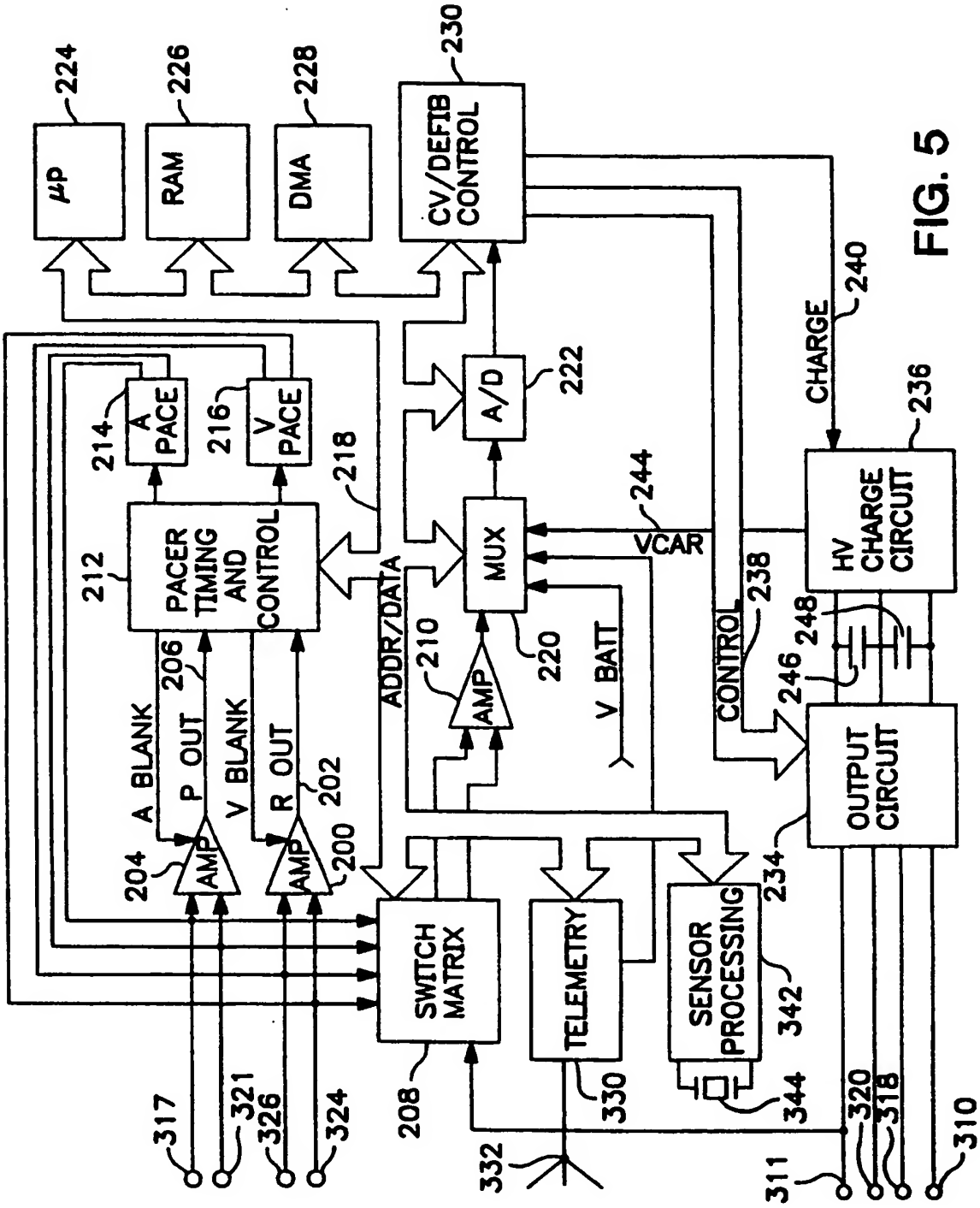


FIG. 5

BNSDOCID: <WO___0051680A1_I_>

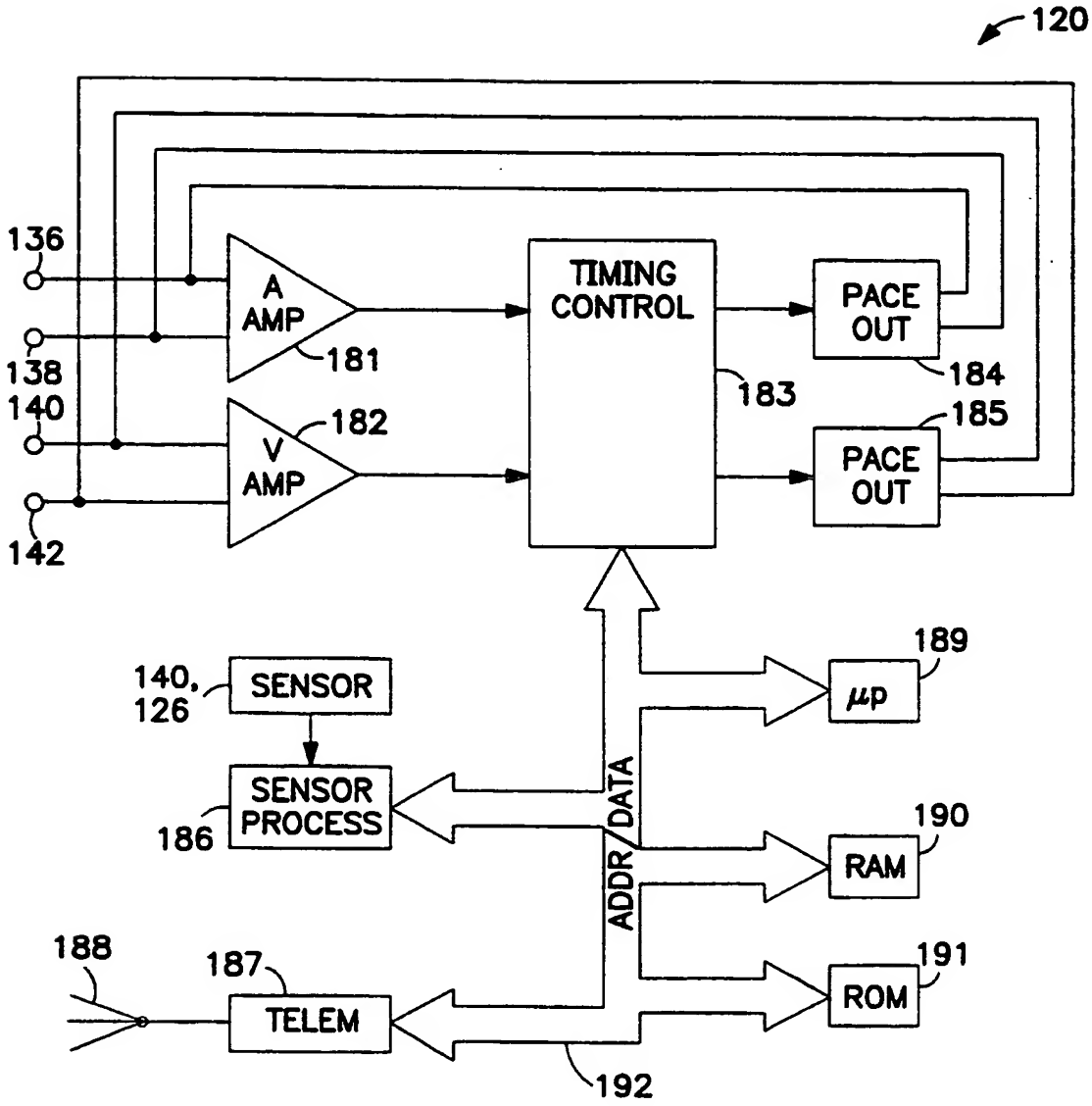


FIG. 6

BNSDOCID: <WO___0051680A1_I_>

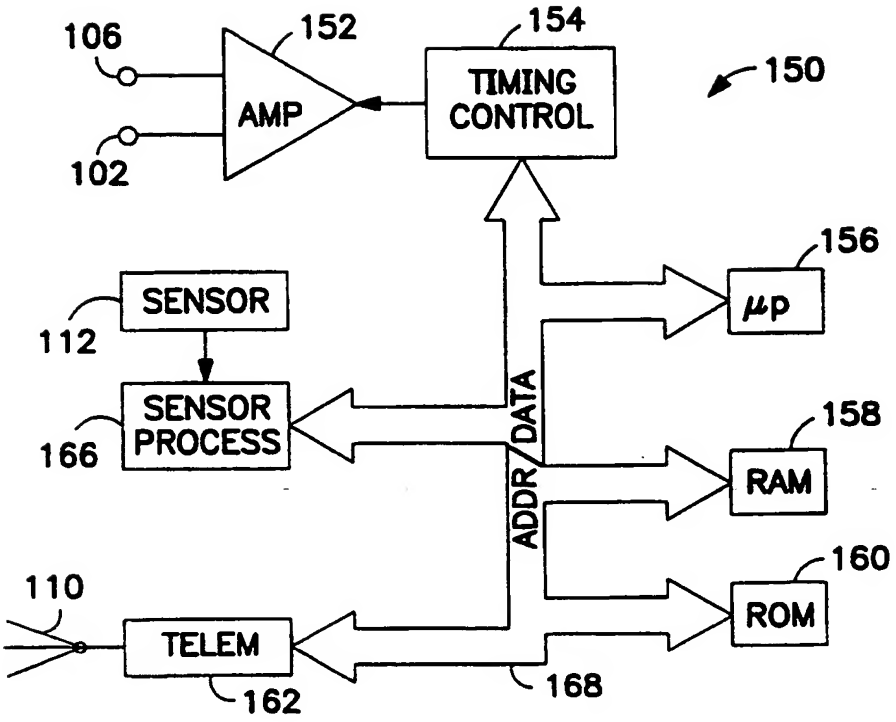


FIG. 7

BNSDOCID: <WO___0051680A1_I_>

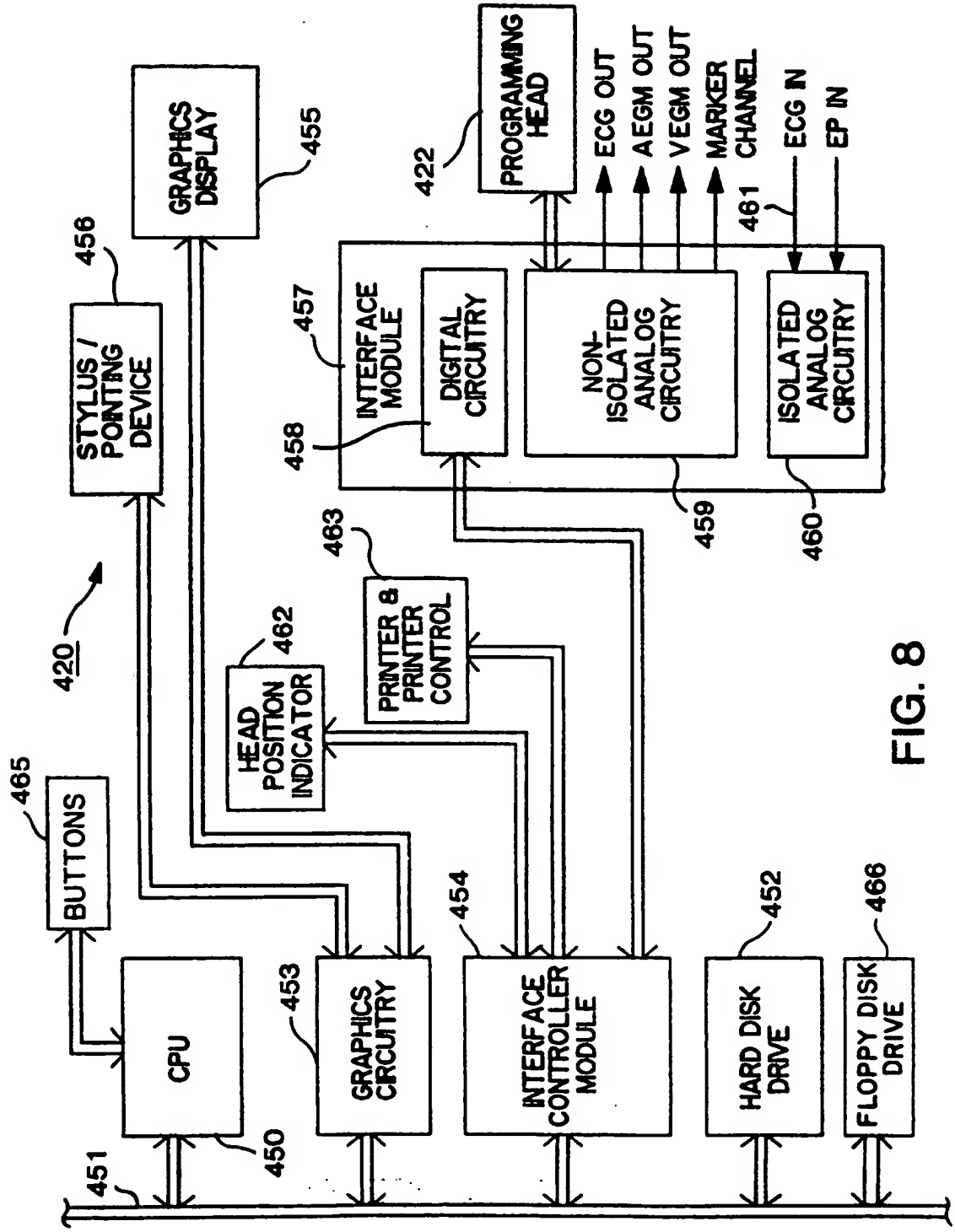
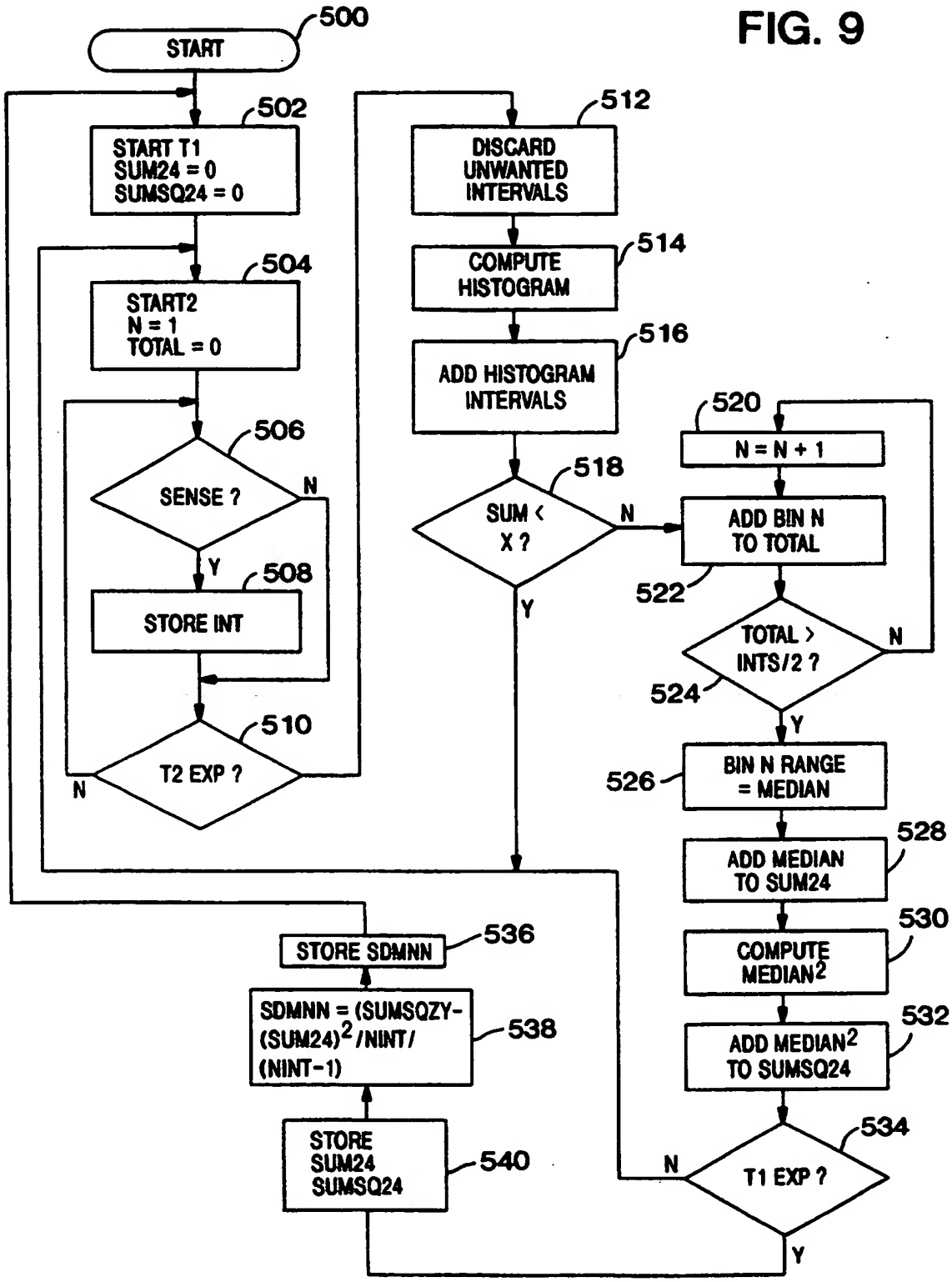


FIG. 8

BNSDOCID: <WO__0051680A1_I_>

FIG. 9



BNSDOCID: <WO___0051680A1_I_>

INTERNATIONAL SEARCH REPORT

Inte onal Application No
PCT/US 00/05185

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61N1/37 A61N1/39

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 749 900 A (SCHROEPPEL EDWARD A ET AL) 12 May 1998 (1998-05-12) cited in the application abstract column 2, line 31 -column 3, line 54 column 6, line 31 - line 47 column 7, line 4 - line 64	1
Y	---	4
Y	US 5 088 488 A (MARKOWITZ HAROLD T ET AL) 18 February 1992 (1992-02-18) cited in the application abstract column 1, line 34 -column 2, line 51	4

	-/--	

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
11 July 2000	18/07/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Ferrigno, A

Form PCT/ISA/210 (second sheet) (July 1992)

BNSDOCID: <WO__0051680A1_I_>

INTERNATIONAL SEARCH REPORT

Inte onal Application No
PCT/US 00/05185

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 514 162 A (BORNZIN GENE A ET AL) 7 May 1996 (1996-05-07) abstract column 5, line 39 -column 6, line 48	1,4
A	US 5 697 959 A (POORE JOHN W) 16 December 1997 (1997-12-16) column 2, line 36 -column 4, line 9	1

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

BNSDOCID: <WO__0051680A1_I_>

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inte onal Application No
PCT/US 00/05185

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5749900 A	12-05-1998	CA 2239364 A	18-06-1998
		WO 9825668 A	18-06-1998
		US 6035233 A	07-03-2000
		EP 0944411 A	29-09-1999
US 5088488 A	18-02-1992	NONE	
US 5514162 A	07-05-1996	NONE	
US 5697959 A	16-12-1997	NONE	

BNSDOCID: <WO___0051680A1_I_>

PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7 : A61N 1/37, 1/39 — A1

(11) International Publication Number: WO 00/51680

(43) International Publication Date: 8 September 2000 (08.09.00)

(21) International Application Number: PCT/US00/05185

(22) International Filing Date: 1 March 2000 (01.03.00)

(30) Priority Data:

60/123,145	5 March 1999 (05.03.99)	US
09/452,533	1 December 1999 (01.12.99)	US

(81) Designated States: CA, JP, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published
With international search report.
With amended claims.

Date of publication of the amended claims:
16 November 2000 (16.11.00)

(71) Applicant: MEDTRONIC, INC. [US/US]; 7000 Central Avenue NE, Minneapolis, MN 55434 (US).

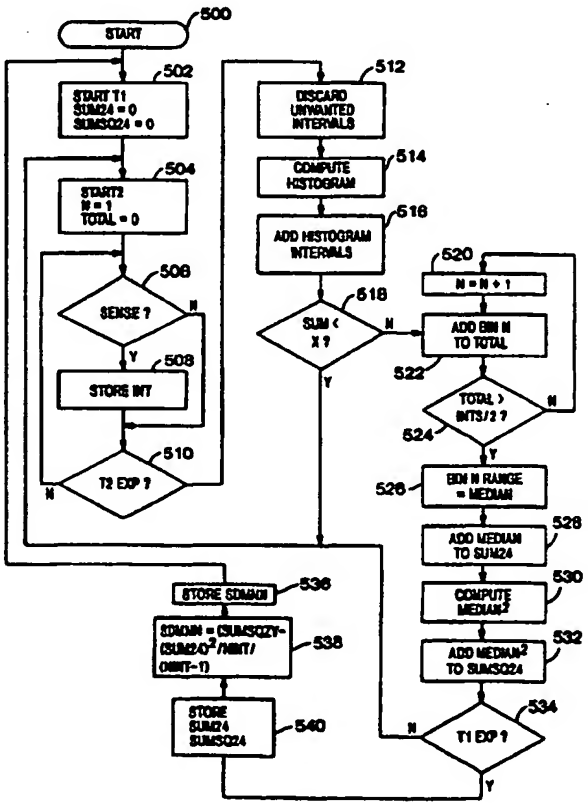
(72) Inventors: PADMANABHAN, Vasant; 8165 Peony Lane North, Maple Grove, MN 55331 (US). OLSON, Walter, H.; 16 Hay Camp Road, North Oaks, MN 55127 (US).

(74) Agents: DUTHLER, Reed, A. et al.; Medtronic, Inc., 7000 Central Avenue NE, Minneapolis, MN 55432 (US).

(54) Title: METHOD AND APPARATUS FOR MONITORING HEART RATE

(57) Abstract

An implantable monitoring device for monitoring a patient's heart rate variability over time. The device includes a cardiac electrogram amplifier, a sensing electrode coupled to an input of the amplifier, timing circuitry, processing circuitry and a memory. The timing circuitry defines successive monitoring periods each extending over a period of hours, the monitoring periods together extending at least over a period of weeks and also defines successive shorter time periods during each monitoring period. The memory stores heart intervals between depolarizations of the patient's heart sensed by the amplifier during the shorter time periods. The processing circuitry calculates median intervals between depolarizations of the patient's heart sensed by the amplifier during the shorter time periods and calculates standard deviations of the median intervals calculated during each monitoring period. The processing circuitry may also reject heart intervals occurring during tachyarrhythmias and calculate median intervals based only on heart intervals not rejected.



BNSDOCID: <WO___0051680A1_IA>

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece			TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	NZ	New Zealand		
CM	Cameroon			PL	Poland		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakstan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

BNSDOCID: <WO___0051680A1_IA>

AMENDED CLAIMS

[received by the International Bureau on 22 August 2000 (22.08.00):
original claims 1-4 replaced by new claims 1-7 (2 pages)]

1. An implantable monitoring device (100) for monitoring a patient's heart rate variability over time, comprising:

a sensing electrode responsive to the patient's heart beats (106, 102);

an amplifier (152) coupled to the sensing electrode; and

a data processor and control circuit (156) coupled to the amplifier and operating in accordance with a set of program instructions, comprising:

(a) a first monitoring period timer (502) having a first timed monitoring interval extending over a period of hours and being resettable to produce a series of first timed monitoring intervals extending at least over a period of weeks;

(b) a second monitoring period timer (504) having a second timed monitoring interval that is shorter in duration than the first timed monitoring period and being resettable to produce a series of second timed monitoring intervals during the first timed monitoring interval;

(c) a heart interval measurement timer (506) actuated by successive heart beats;

(d) a memory (158) coupled to the heart interval measurement timer and having storage locations for heart interval measurements obtained during the second timed monitoring interval;

(e) a calculator (514) of a median heart rate for the patient during each of the second timed monitoring intervals and using the stored heart interval measurements; and

(f) a calculator (528, 530, 532) of a standard deviation of the calculated median heart rates of the patient occurring within the first timed monitoring interval.

2. A device according to claim 1, wherein the memory stores heart interval measurements that are in excess of a heart interval identified as a tachyarrhythmia.

3. A device according to claim 2, further comprising a calculator (518) of a total duration of the stored heart interval measurements and wherein the median heart rate

BNSDOCID: <WO__ 0051680A1_IA>

calculator calculates a median heart rate only if the total duration of the stored heart interval measurements is in excess of a required duration.

4. A device according to claim 1, wherein the memory further comprises a histogram having multiple bins and each bin contains heart interval measurements within a predetermined range.

5. A device according to claim 4, wherein the median heart rate calculator successively adds together the number of intervals stored in successive bins of the histogram until a sum is reached which is equal to or greater than one-half of the total number of heart interval measurements in all bins of the histogram.

6. A device according to claim 5, wherein the median heart rate calculator, in response to a sum of the added together stored intervals exceeding one-half of the total number of heart rate interval measurements in the histogram bins, designating as a median heart rate a heart interval measurement within the last histogram bin added having the number of intervals stored therein most recently added to the sum.

7. A device according to claim 1, wherein the median heart rate calculator comprises a routine of instructions within the set of program instructions having an output that is a median heart rate for the patient during each of the second timed monitoring intervals and using the stored heart interval measurements; and wherein the standard deviation calculator comprises a routine of instructions within the set of instructions having an output that is a standard deviation of the calculated median heart rates of the patient occurring within the first timed monitoring interval.

BNSDOCID: <WO__0051680A1_IA>